Topics in
Primary Care Medicine

Refer to: Lo B: The diagnosis of pulmonary embolus (Topics in Primary Care Medicine). West J Med 1982 Jun; 136: 542-545

The Diagnosis of Pulmonary Embolus

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In this issue The Western Journal of Medicine *begins a new series, "Topics in Primary Care Medicine," that will present articles on common diagnostic or therapeutic problems encountered in primary care practice. These articles will address such frequently occurring problems as dizziness, pruritus, insomnia, shoulder pain and urinary tract infections. These problems usually do not fall into well-defined subspecialty areas and are rarely discussed thoroughly in medical school, house staff training, textbooks and journals. Often the pathophysiology is poorly understood and clinical trials to assess the effectiveness of diagnostic tests or therapies are often lacking. Nevertheless, these problems confront practitioners with practical management questions.*

The articles in this series will discuss new tests and therapies and suggest a reasonable approach even when definitive studies are not available. Each article will have several general references for suggested further reading. We hope this new series will be of interest and we welcome comments, criticisms and suggestions.

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Series' Editors

THE DIAGNOSIS of pulmonary embolism (PE) is a common, important and difficult problem for primary care physicians. It is important not to miss the diagnosis inasmuch as the mortality of untreated PE is 25 percent, compared with a mortality of 2 percent to 9 percent in patients treated with heparin.

Establishing the diagnosis of PE can be difficult. Findings on history, physical examination and laboratory tests are not specific. The results of lung scanning may not be conclusive. Angiography provides definitive diagnosis but is invasive and costly.

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Because PE is a serious disease with nonspecific presentations, the physician must consider the diagnosis and work up many patients who in fact do not have PE. In a prospective multicenter study, over 94 percent of patients suspected of having PE were found not to have it. PE should be efficiently ruled out in these patients. Falsely positive diagnoses have serious consequences because the risk of major bleeding from heparin is as high as 8 percent and from warfarin, 17 percent.

Clinical Evaluation

The clinical presentation of PE is varied and not specific (Table 1). Predisposing factors include deep venous thrombosis, embolization, chronic pulmonary or cardiac disease, estrogen use or pregnancy and cancer. The most common

ABBREVIATIONS USED IN TEXT

COPD=chronic obstructive pulmonary disease
PE=pulmonary embolism
P_{O_2}=oxygen partial pressure
V/Q=ventilation-perfusion

symptoms are dyspnea, pleuritic pain and cough. In patients with prior cardiac or pulmonary disease, a large pulmonary embolus may cause shock and congestive heart failure. More subtle presentations include worsening of heart failure or onset of atrial fibrillation.

Tachypnea is a common finding on physical examination. Tachycardia, increased second pulmonic heart sound, fever, deep venous thrombosis and pleural rub are less frequently found.

Laboratory Studies

Hypoxemia occurs in 88 percent of cases. Abnormalities in lactate dehydrogenase (LDH), serum aspartate aminotransferase (formerly glutamic-oxaloacetic transaminase, SGOT) and bilirubin usually are not helpful in establishing the diagnosis. Although the chest x-ray studies are abnormal in 50 percent to 88 percent of cases, the findings of effusion, atelectasis, infiltration and an elevated hemidiaphragm are not specific. Similarly, though the electrocardiogram is abnormal in 87 percent of cases, the findings of tachycardia and ST segment changes are not specific. Acute cor pulmonale, said to be diagnostic of PE, is found in only 26 percent of cases.

A normal result on a sensitive* test when the clinical suspicion is low helps rule out the diagnosis. For example, in a young woman with tachypnea and anxiety but no risk factors, the likelihood of PE certainly is no greater than the 6 percent prevalence in the multicenter study. If she has an oxygen partial pressure (P_{O_2}) greater than 80 mm of mercury, this probability is reduced to 2 percent. In another patient where the clinical suspicion of PE is higher (for example, if the prior probability is estimated to be 25 percent), a P_{O_2} greater than 80 mm of mercury reduces the probability of PE to 10 percent.

But abnormal results of sensitive tests do not establish the diagnosis of PE. Because these tests are not specific,† further evaluation is needed. Specificity has not been rigorously studied; Table 1 lists reasonable estimates. For example, the only reported specificity for hypoxemia is 34 percent.

*The sensitivity of a test is the probability of having a positive result in a patient with the disease.

†The specificity of a test is the probability of having a negative result in a patient who does not have the disease.

TABLE 1.—*Sensitivity and Specificity of Findings in Pulmonary Embolism*

Findings	*Sensitivity (percent)*	*Specificity (percent)*
Symptoms		
Dyspnea	70-84	<50
Pleuritic pain	42-74	50-75
Cough	42-53	50-70
Hemoptysis	14-30	50-70
Predisposing factors	94	50-70
Physical findings		
Tachypnea >24	37-92	50-70
Tachycardia >90	44-53	50-70
Increased P_2	53	50-70
Fever	43-50	50-70
Deep venous thrombosis	30-33	50-70
Pleural rub	14	50-70
Laboratory tests		
P_{O_2} <80 mmHg	88	<50
Abnormal chest x-ray	50-80	<50
Abnormal electrocardiogram	87	<50
Lung scanning		
Abnormal perfusion scan	99	<50
Abnormal V/Q scan	36-99	73-98*
Abnormal angiogram	98	>99

P_2=pulmonic second sound; P_{O_2}=oxygen partial pressure; V/Q=ventilation perfusion

*Depends on the pattern of abnormality.

Lung Scan

Lung scanning is usually the next step after clinical evaluation and simple laboratory tests. In a perfusion scan, images are taken after the injection of technetium-labeled albumin. Defects represent areas of decreased perfusion. In a ventilation scan, images are taken after inhalation of xenon or krypton. Defects represent areas of decreased ventilation. A ventilation-perfusion (V/Q) scan compares ventilation images with perfusion images.

The diagnostic accuracy of lung scans, however, is controversial. All reported series suffer from selection bias because not all patients having scans also have pulmonary angiograms to confirm the diagnosis. Observers differ substantially in interpreting scans. In one series, five experts could agree on the classification of perfusion scans into four categories in only 40 percent of cases. Interobserver agreement on V/Q scans has not been studied.

Perfusion scans are highly sensitive for PE (Table 1), so that *a normal perfusion scan effectively rules out the diagnosis.* Furthermore, if a scan shows multiple subsegmental perfusion de-

fects, there is a low (7 percent to 9 percent) probability of finding PE on angiography. However, other abnormal findings on perfusion scans are not specific for PE and must be evaluated further.

V/Q scans increase the diagnostic accuracy of abnormal perfusion scans in some groups of patients. Patients with multiple large perfusion defects unmatched by ventilation defects have a high probability of having PE on angiography. If the perfusion defects are lobar, the probability of PE is 92 percent to 100 percent. If the defects are segmental, the probability of having PE is 85 percent to 95 percent. On the other hand, patients with single or multiple perfusion defects that are matched by ventilation defects have a low (0 percent to 9 percent) probability of having PE on angiography. Angiography usually is not necessary in these high and low probability groups of patients.

Difficulties With Lung Scans

The accuracy of scans with defects corresponding to infiltrates on x-ray is controversial. One series suggests that if the perfusion defects are larger than the x-ray infiltrates, the probability of PE is high, whereas if they are smaller, the probability is low. However, the series is small and interpretations of "greater" and "smaller" may be unreliable. A prudent course is to obtain angiograms in these patients.

Other findings on V/Q scan have an intermediate (20 percent to 40 percent) probability of PE. Examples are diffuse ventilation abnormalities due to chronic obstructive pulmonary disease (COPD) and scans with multiple perfusion defects, some matched by ventilation defects and others unmatched. This intermediate probability group requires angiography to confirm or exclude the diagnosis.

In some circumstances the physician may decide to omit lung scans and to proceed directly to angiography after clinical evaluation. Examples are patients with COPD or radiographic infiltrates who are suspected of having PE.

Technical details may influence the ordering of scans. Some centers recommend initially ordering a V/Q scan rather than a perfusion scan because a high-quality xenon ventilation scan cannot be obtained for several hours after a perfusion scan. If the clinical suspicion of PE is low, however, it is reasonable to order a perfusion scan alone as a first step. If it is negative, the patient is spared an unnecessary procedure. If the perfusion scan does not rule out PE, heparin can be given until more definitive diagnosis with ventilation scan or angiogram is obtained. It is claimed that krypton ventilation scans may solve this problem because they have high resolution even if done immediately after perfusion scans. However, krypton is more expensive, not widely available and not rigorously studied.

Pulmonary Angiography

Angiography is considered the "gold standard" for definitive diagnosis of PE. It is highly specific and sensitive (Table 1). Intraluminal filling defects are diagnostic of PE and a negative angiogram rules it out. However, falsely negative angiograms may occur, as 1.5 percent to 2.5 percent of patients with negative angiograms will have later angiographic or autopsy evidence of PE. Falsely negative angiograms due to resolution of the embolus are rare if the test is done within 48 hours of the onset of symptoms. The interobserver reliability of angiogram readings is excellent, with disagreement in fewer than 6 percent of cases.

Although angiography provides definitive diagnosis, it is impractical to do angiograms on all patients suspected of PE. Most angiograms would be negative because PE is overdiagnosed clinically. High quality studies cannot be obtained at all hospitals. Moreover, angiograms are expensive, costing from $500 to $1,000 depending on the number of films taken, compared with $175 for a V/Q scan.

Angiograms also involve some risk to patients. The mortality of angiography is under 0.5 percent, with intractable shock in patients who have elevated right heart pressures accounting for many deaths. Significant morbidity, such as cardiac arrest, symptomatic arrhythmias, right ventricular perforation and anaphylaxis, occur in 1.6 percent to 2.3 percent of cases. These data were gathered at centers doing more than 80 procedures a year; the complication rate at less experienced centers probably is higher.

Individualizing the Workup

The workup for PE must be specific for each patient. In a particular hospital, some tests may not be available or local experience may not match the results reported in the literature. Also the values of the physician and patient, especially

their attitudes toward risk and uncertainty, must be taken into account. In many circumstances a 90 percent probability of PE may be sufficient reason to begin therapy. In the following situations, however, the physician or patient may desire the greater diagnostic certainty that angiography offers compared with lung scanning: (1) The patient is at high risk for bleeding from anticoagulation because of advanced age, recent surgical procedures, trauma or bleeding or hemostatic defects. (2) Thrombolytic therapy, which increases the risk of major bleeding, is considered. Angiography should be done via an antecubital rather than a femoral approach, so that bleeding at the site can be controlled by direct pressure. (3) Interruption of the inferior vena cava is considered.

New Approaches

One suggested approach to diagnosing PE is to study the legs with venography or impedance plethysmography and to initiate anticoagulation if deep venous thrombosis is present, even though the presence of PE may be uncertain. However, the incidence of false-negative diagnoses with this approach has not been studied rigorously. Another approach is to measure fibrin and fibrinogen degradation products or platelet release factors. Again, this approach has not been rigorously studied.

Summary

Clinical findings and simple laboratory tests can suggest PE, but positive findings must be confirmed. A normal perfusion scan effectively rules out PE. Multiple lobar or segmental V/Q mismatches have a high probability of PE, but matched ventilation and perfusion defect(s) have a low probability of PE. Arteriography will be necessary with other V/Q scan results or when greater diagnostic certainty is desired. Treatment must be individually tailored according to the details of the case, the availability of tests and the values of the patient and physician.

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